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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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EXAMINER

ANGELL, JON E

ART UNIT PAPER NUMBER

1635

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|--------------------------------------|--------------------------------------|--|
| Office Action Summary | Application No. 10/035,300 | Applicant(s) EALICK ET AL. | |
| | Examiner Jon Eric Angell | Art Unit 1635 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-56 is/are pending in the application.
- 4a) Of the above claim(s) 3,5,8,34-53 and 55 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4,6,7,9-33,54 and 56 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>1/28/03</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This Action is in response to the communication filed on 5/21/04. Claims 1-56 are currently pending in the application and are addressed herein.

Election/Restrictions

Applicant's election with traverse of Group XX in the reply filed on 5/21/04 is acknowledged. The traversal is on the ground(s) that (1) the Examiner has in practice amended the claim scope from "a mutant purine cleaving enzyme" into a recitation of species corresponding to each of the Groups I-XX and these different species should be no more than a species election; (2) the Examiner has failed to define compositions with properties so distinct as to warrant a separate examination and search; and (3) the searches required for groups I-XX can be made without serious burden.

Regarding argument (1), the Examiner partially accepts the Applicants argument, and in response the restriction requirement is modified such that claims 1, 2, 4, 7, 14, 19, 20, 22, 27 and 33 are now "linking claims" that link inventions I-XX.

Regarding the linking claims, it is noted that the restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s). Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the

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continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Regarding arguments (2) and (3), the Examiner disagrees with the Applicants argument because the groups encompass enzymes that have different chemical structures (sequences) and have different functions. Although all of the compositions encompass “enzymes” it is noted that enzymes is a very broad class of molecules that have different structures and functions. For instance, as in the instant case, some enzymes can be hydrolases while other enzymes can be phosphorylases. Hydrolases and phosphorylases, although both enzymes, are patentably distinct from each other because they have different chemical structures and different functions. Furthermore, the searches required for each is distinct because the search of the sequence databases requires the search for each of the distinct structures, where each structure is considered a separate search. Additionally, the searches of the literature and patents databases would require different search terms, such as “hydrolase” and “phosphorylase” and the particular species that the enzyme is from, evidence that the searches for each groups is not the same. Also, the different groups have different sub-classifications, prima facie evidence of a serious search burden.

Therefore, the restriction requirement has been modified as indicated above such that the linking claims are not limited to the elected subject. With respect to the linking claims, it is noted that the linking claims are only examined herein to the extent of their non-allowance, as indicated above.

The modified restriction requirement set forth above is deemed proper in view of Applicants arguments; therefore, the modified restriction requirement is deemed final.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 1/28/03 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 2, 4, 6, 7, 9-3, 54 and 56 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 1 reads on a nucleotide sequence; however, the claim does not explicitly indicate that the nucleotide sequence is isolated. Therefore, the claims encompass a naturally occurring nucleotide sequence, which is non-statutory subject matter. It is noted that claims 14-21 are drawn to a vector comprising the nucleotide sequence of claim 1. Claims 1-14 and 27-33 encompass a naturally occurring vector including a virus (note: recombinant virus does not limit the claim to non-naturally occurring because all nucleic acids, including viruses, are considered recombinant by nature), and as such, these claims are drawn to non-statutory subject matter. Claims 22-26 are drawn to a host cell transformed with a vector comprising the nucleotide sequence of claim 1. Since the vector can be naturally occurring, the cell transformed with the vector could also be a product of nature, and

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thus, non-statutory subject matter. Claim 54 and 56 are drawn to a commercial kit comprising a vector or recombinant virus wherein the vector or recombinant virus comprise nucleotide sequences. Since the vector and recombinant virus could be a naturally occurring product, the claims encompass non-statutory subject matter.

Amending the claim to clearly limit the claims to isolated nucleic acid sequences such that the claims do not encompass naturally occurring nucleic acid sequences would obviate this rejection.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9, 11, 15-18, 23-26, 28-31, 54 and 56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims recite the phrase “depicted as” when referring to particular sequences indicated in the claims. However, it is not clear if “depicted as” is intended to mean “comprising”, “consisting of”, or something else. It is noted that Merriam –Webster online Dictionary (www.m-w.com) defines depicted as, “to represent by or as if by a picture”. Therefore, the claims could encompass sequences that are merely “represented by” the sequences identified, although they may be different from the identified sequences. It is suggested that the claims be amended to clearly indicate that the sequences either “comprise” or “consist” of the identified sequences.

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Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claim recites the phrase, “wherein the different biological activity is greater biological activity” (emphasis added). Here, the phrase “greater biological activity” renders the claim indefinite because it is not clear what “greater biological activity” means, or how “greater biological activity” is determined. Specifically, since there is no specific reference biological activity indicated, it is unclear what would constitute “greater biological activity”, (i.e. “greater” relative to what?). Amending the claim to clearly indicate that the different biological activity is greater biological activity relative to (or compared to) wild-type biological activity would obviate this rejection.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4, 6, 7, 13, 14, 19-22, 27, 32 and 33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Written Description Guidelines for examination of patent applications indicates, “the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e. structure or other physical and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus.” (See MPEP 2100-164)

Instant claims 1, 2, 7, 14, 19, 20, 22, 27 and 33 are drawn to a genus of nucleotide sequences that encode mutant purine cleaving enzymes having different biological activity than a wild-type purine cleaving enzyme. (Note: claim 2 specifically indicates that different biological activity is greater biological activity). As such the claims are drawn to a genus of molecules that encompass an indefinite, but most-likely, huge number of different species molecules wherein the species can vary greatly in chemical structure and function. For instance the genus encompasses mutants which have been mutated such that they no longer cleave the same molecule as the wild-type enzyme, that is, mutants which no longer have the same enzymatic activity as the wild type. An example would be a purine nucleoside phosphorylase mutated to be a purine nucleoside hydrolase, deaminase, methylase, etc. Therefore, the claims encompass a genus of molecules that includes possibly thousands or millions of different molecules considering every possibly mutant purine cleavage enzyme encompassed by the claims, including mutants and allelic variants which have yet to be discovered. The specification, however, has not provided sufficient written description of the genus of molecules encompassed by the claims

Instant claims 4 and 6 limit the mutant purine cleaving enzymes to purine nucleoside phosphorylases (claim 4) and *E. coli* purine nucleoside phosphorylases (claim 6). These claims are still drawn to a genus of molecules that encompass a huge number of different specific species. For instance, claim 4 encompasses mutant purine nucleotide phosphorylases (PNP) of any biological species that have different chemical structures compared to their wild-type PNP counterpart. As such, the claims encompass PNPs which have not been described and includes mutants and variants that have yet to be discovered. Similarly claim 6 is drawn to a genus of *E. coli* PNPs that are mutants of the wild-type *E. coli* PNP. Again, this genus encompasses *E. coli* PNPs which have not been described and includes mutants and variants that have yet to be discovered, including naturally occurring allelic variants as well as mutants thereof.

Claims 13, 21 and 32 are drawn to a nucleotide sequence encoding a mutant *E. coli* PNP containing a complete open reading frame that encodes one of 20 point mutations. It is noted, that these claims encompass "a complete open reading frame" which merely indicates that the open reading frame comprises a start codon and a stop codon such that the open reading frame that has one of the specifically indicated mutations. Therefore, the claims still encompass a vast number of different mutations including truncations (which are still complete open reading frames) that have the indicated mutations. Furthermore these claims encompass naturally occurring allelic variants.

The specification has not adequately described a representative number of species, in view of vast breadth of molecules encompassed by the claims. As such the disclosure does not meet the written description requirement. The specification has disclosed a number of specific mutations of an *E. coli* PNP enzyme that have either a greater or lesser phosphorylase activity

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compared to one specific wild-type E. coli PNP. The specific point mutations of E. coli PNP described in the specification are disclosed in Table I (see p. 12). It is noted that only **ONE** of the disclosed mutant E. coli PNPs have a phosphorylase activity that is greater than the wild-type phosphorylase activity: A157V.

Additionally, the instant claims are rejected under 35 U.S.C. 112, first paragraph, in view of the written description rejection above, because the specification, while being enabling for an isolated nucleic acid sequence that is SEQ ID NO. 1, SEQ ID NO. 3, or a specific point mutation of E. coli PNP as disclosed in Table I (p. 12 of the specification) (as well as vectors comprising these specific sequences, host cells comprises the specific sequences and kits comprising the specific sequences) does not reasonably provide enablement for the full scope encompassed by the claims (i.e. any mutation of E. coli PNP). Considering the vast breadth of molecules encompassed by the claims and the limited number of molecules which have actually been described in the specification (indicated above), the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 7, 14, 20 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Maynes et al. (Biochem. J., 1999).

The instant claims are drawn to a nucleotide sequence encoding a mutant purine cleavage enzyme having different biological activity than a wild-type purine cleavage enzyme (claim 1); wherein the different biological activity is greater biological activity (claim 2); wherein the mutant purine cleavage enzyme is a nucleoside phosphorylase (claim 4); wherein the enzyme has different biological activity cleaving a nucleoside analog than a wild-type enzyme (claim 7); wherein the nucleotide sequence is in a vector (claim 14); wherein the vector is a plasmid (claim 20); wherein a host cell is transformed with the vector (claim 22).

Maynes teaches a nucleotide sequence encoding a mutant purine cleavage enzyme that has different biological activity than the wild-type enzyme (e.g., see abstract, p. 586 first column, etc.); wherein the different biological activity is greater biological activity (e.g., see abstract, Table 1); wherein the mutant purine cleavage enzyme is a nucleoside phosphorylase (e.g., see abstract); wherein the enzyme has different biological activity cleaving a nucleoside analog than a wild-type enzyme (e.g., see abstract, Table 1, Table 3); wherein the nucleotide sequence is in a vector, wherein the vector is a plasmid, wherein a host cell is transformed with the vector (e.g., see p. 586 first column, etc.).

Conclusion

No claim is allowed.

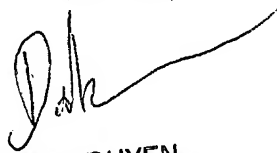
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon Eric Angell
Art Unit 1635



DAVE T. NGUYEN
PRIMARY EXAMINER